Instructions: *Use Times New Roman font size 11, 1.0 pt text space, and* ***maximum three A4 pages****, including any figures.*

Name or type of instrument	**850 MHz NMR Parallel Steering Unit**
Unit	Swedish NMR Centre UMU node
Platform	Integrated Structure Biology
Applicant (Head of Unit)	Göran Karlsson
E-mail address	goran.karlsson@nmr.gu.se
Instrument, acquisition cost (kSEK)	8 000
Funding applied for (kSEK)	4 800

Description of the instrument

The 850 MHz NMR at UMU (s. Fig. 1) is a SciLifeLab flagship instrument for advanced solid-state/solution NMR experiments using unique Cryo-NMR liquid probes, ultra-fast solid-state (111 kHz) MAS NMR probes and high-throughput robotic sample changers. Since its installation in 2012 we upgraded it with novel NMR probes (2014, 2021). But the **electronic console** controlling the NMR and enabling sophisticated experiments remained unchanged. Now the console (s. Fig. 1) is nearly at the end of its lifetime, suffering not only increasing repair costs but also failing to execute newly developed experiments, or to control forthcoming signal detectors. Since Bruker's change to a new console concept (NEO), NMRs with older consoles are excluded from those advanced developments in all aspects of life sciences. Therefore, we apply here for a state-of-the-art steering unit for the SciLifeLab 850 MHz solid/liquid NMR flagship to continue to compete internationally by offering Swedish Academia/Industry further access to world class equipment and expertise in coming years.

The total cost is ca. 8 MSEK for this NEO-type steering unit (Bruker, sole supplier), offering superb novel capabilities including parallel transceivers with simultaneous detection of different nuclei (e.g. ^{15}N, ^{13}C, ^{1}H). This will allow our most recently installed solid-state probes (-2021) to exploit their full potential. **This essential investment** will ensure that this national NMR flagship will again become a state-of-the-art part of ScilifeLab's ISB (Integrated Structure Biology) platform and not fall behind the other top-modern ISB based approaches to determine atomic resolution 3D structures of biomolecules, and tackle demanding problems in all areas of life sciences.

Fig. 1: Solid/Liquid 850 MHz NMR at the UMU NMR node of SciLifeLab's ISB platform: Steering unit on the left (behind glass doors of air-conditioned compartment).

Statement of need

Operations

The use of the 850 MHz NMR for liquid as well as solid-state NMR has been very high, with many projects of national interest ranging from structural and functional work under the ISB SciLifeLab platform to numerous academic and industrial projects with customers from AstraZeneca and Sartorius to FOI and smaller enterprises; on topics covering life sciences, medicine (including Covid applications), metabolomics and material sciences. With the UMU node's expertise in solid-state NMR on complex biological systems, the focus of many projects (membrane proteins, protein aggregates, but also drug isomorphs) has become to use the Sweden-unique 0.7 mm-diameter ultra-fast MAS NMR techniques (Fig. 2). At 111 kHz spinning speed, this probe offers unique capabilities in structural work. In addition, the use as high-field liquid NMR machine with its advanced cryo-probes has been increasing for work on biological questions at national, international and local level. Furthermore, using unique equipment for isotopomer quantification, the instrument is used for topics in forensics (cooperation with FOI), environment and Planetary Biology, thus contributing to this SciLifeLab mission area.

Fig. 2: The Sweden unique 0.7 mm MAS ultra-fast MAS probe (111 kHz) at 850 MHz NMR for solid-state applications for academia and industry.

Equipping this national 850 MHz flagship with the steering unit with the novel NEO architecture will not only make sure that the 850 MHz NMR is national-wide available in the next years but it will also provide new capabilities in form of advanced NMR experiments, as installation of new probes and accessories relies on those new NEO consoles. This will expand tremendously the capacity and output of the instrument, since much more advanced experiments can be implemented.

A new technology for NMR: The new NMR console design NEO features a novel architecture which offers for the first time the capability of multi-receiver pulse sequencing and complex experimental design. This enables the simultaneous observation of different nuclei in molecules of interest by exploiting modern multi-dimensional approaches with reduced acquisition time due non-linear sampling.

This technology opens innovatice and exciting developments in many key areas of SciLifeLab: In structural biology, this technology in combination with our advanced liquid Cryo-probes or solid-state ultrafast MAS probes can extract structural and dynamics information for more complex biomolecules and their aggregates by using multi-dimensional strategies while reducing NMR times significantly (1). Second, this console allows the use and development of NMR super-sequences for studying complex mixtures as e.g. in metabolomics (2), and finally, it opens access to study novel materials including complex biomaterials, by exploiting natural isotope abundance of the NMR visible nuclei (3).

This new NMR console architecture will open new avenues for the next level of information rich NMR experiments. Therefore, it will clearly strengthen the ISB platform significantly not only as a method on it is own but also as a key method in collaboration with Cryo-EM-, X-ray- and MS-based methods, all under the ISB umbrella. In addition, it will be capable of carrying out advanced studies of samples from biospecimen to novel inorganic materials for the Swedish and international community.

An upgrade to this new console architecture NEO would ensure top performance of the high-value investment of the 850 MHz magnet for another decade to come with a limited amount of money.

Productivity and development

The new parallel steering unit will significantly increase capacity in running advanced molecular NMR applications with most recently developed experiments on an internationally competitive level. In addition, it will ensure not only another 10 years as national NMR flagship for solid-state and liquid NMR in most sciences, but will also lay the foundation to fully integrate the next generation of hardware NMR development with respect to probes and accessories, something already not possible anymore. The 850 MHz NMR can then also complement - with its solid-state capabilities - the solution NMR at the GU SNC node with its 900 MHz liquid NMR; to combine their power for complex structural questions, and to run combined large cohorts of samples ranging from clinical metabolomics to drug screening. We have recently demonstrated this synergy between the nodes in the case of COVID-related projects. Finally, the solid-state capabilities are also an ideal complement to the DNP Facility at GU (first in Scandinavia).

Use

The system will be available to the entire SciLifeLab community, to all national academic and industrial users, to the main SNC node at GU, and to local users in Umeå affiliated with UMU, SLU (Umeå), the university hospital (NUS) and various companies. In addition, we also serve RISE and FOI and run international projects as collaborations or as service. As service with an upgraded 850 MHz and state-of-the-art capabilities and expertise, we provide significant input to other SciLifeLab units, e.g. CBCS, DDD, Swedish Metabolomics Platform, and to the national MAXLAB IV and ESS infrastructures.

Funding

As seen in the platform instrument inventory (not shown here) the upgrade is urgently needed to avoid being technology outdated in the years to come.

The extent of local use (~35-40%) suggests a high degree of co-funding. The total cost of the upgrade is ca 8 MSEK for the state-of-the art NEO steering unit with full liquid and solid-state NMR capabilities and fully automated high-throughput sample changer. Of the total cost, 3.2 MSEK will be co-funded by the UMU NMR platform together with UMU's central level and private foundations. The requested funding, 4.8 MSEK, is required to cover the major financial burden for this high-end equipment. The kindly asked support for the purchase of an 850 MHz console is part of a continuous development of NMR instrumentation and is a crucial necessity to stay competitive at the national and international level, and to provide state-of-the-art support in coming years to the entire Swedish community.

References

1. T. Gopinath et al. "PHRONESIS: A One-Shot Approach for Sequential Assignment of Protein Resonances by Ultrafast MAS Solid-StateNMR Spectroscopy." ChemPhysChem (2022) 23, e2022001
2. C. Lhoste et al. "Ultrafast 2D NMR for the analysis of complex mixtures." Progress in Nuclear Magnetic Resonance Spectroscopy 130–131 (2022) 1–46
3. E. Kupce et al. "New NOAH modules for structure elucidation at natural isotopic abundance." Journal of Magnetic Resonance 307 (2019) 106568.